



# The outcome of surgical mitral valve repair with loop-in-loop technique in dogs with different stage myxomatous mitral valve disease



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## KEYWORDS

Degenerative mitral valve disease;  
Surgical technique;  
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**Abstract** *Objectives:* Surgical mitral valve repair is a possible option for dogs with myxomatous mitral valve disease. However, information on surgical results and postoperative echocardiography is limited. This study aimed to verify the stage-specific surgical results of mitral valve repair and postoperative echocardiographic changes for two years following surgery.

*Animals:* Adult dogs (n = 55) treated with surgical mitral valve repair using the loop-in-loop technique were included in this study. Medical records were retrospectively reviewed.

*Results:* Ninety percent of cases (50/55) survived to discharge, which survival was significantly decreased in myxomatous mitral valve disease advanced-stage dogs, Stage B2 (n = 14): 100%, Stage C (n = 27): 96.2%, and Stage D (n = 14): 71.4%. Significant reductions of overall heart size (vertebral heart score: preoperative 11.4 vs. post one month 10.2,  $P < 0.001$ ), left atrium (left atrium to aortic root ratio: preoperative 2.3 vs. post one month 1.5,  $P < 0.001$ ) and left ventricle (left ventricular end-diastolic diameter [normalized for bodyweight]: preoperative 2.2 vs. post one month 1.5,  $P < 0.001$ ) were documented one month after surgery, showing successful management of mitral regurgitation. All medications for mitral valve disease were discontinued three months after surgery. The recurrence of mitral regurgitation was not evident during the two-year follow-up period.

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**Conclusions:** Surgical mitral valve repair with the loop-in-loop technique is associated with significant decreases in indices of cardiac size at one-month post-repair. Disease stage influences operative survival after surgical mitral valve repair. © 2022 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

### Abbreviations

|       |                                   |
|-------|-----------------------------------|
| AF    | atrial fibrillation               |
| ePTFE | expanded polytetrafluoroethylene  |
| IVSH  | inter ventricular septum hematoma |
| LA    | left atrium                       |
| MMVD  | myxomatous mitral valve disease   |
| MR    | mitral regurgitation              |
| PH    | pulmonary hypertension            |
| TR    | tricuspid regurgitation           |

## Introduction

Surgical mitral valve repair can be beneficial for dogs with various staged myxomatous mitral valve diseases (MMVDs) according to consensus guidelines by the American College of Veterinary Internal Medicine [1]. However, published literature on the results of canine mitral valve repair is limited. In addition, information for patient selection, such as perioperative risk factors, disease-specific surgical results, and echocardiographic changes, is limited. In this study, the results of surgical mitral valve repair with radiographic and echocardiographic follow-up are provided, and perioperative complications that are useful for future case selection are described.

## Animals, materials and methods

All dogs that underwent mitral valve repair surgery at VCA Japan Shiraishi Animal Hospital between July 2019 and November 2021 were enrolled in this retrospective study. The medical records of all dogs ( $n = 55$ ) enrolled in this study were reviewed, with the following information collected for each patient: age; breed; disease stage; concurrent disease; medical treatment history; duration of anesthesia; cardiopulmonary bypass time; aortic cross-clamp time; grade of cardiac murmur; vertebral heart score (VHS); echocardiographic variables; renal values and electrolyte values on blood test; perioperative complications; death; cause of death. The VHS ([reference,  $<10.6$ ]), ratio of the left atrial dimension to the aortic annulus

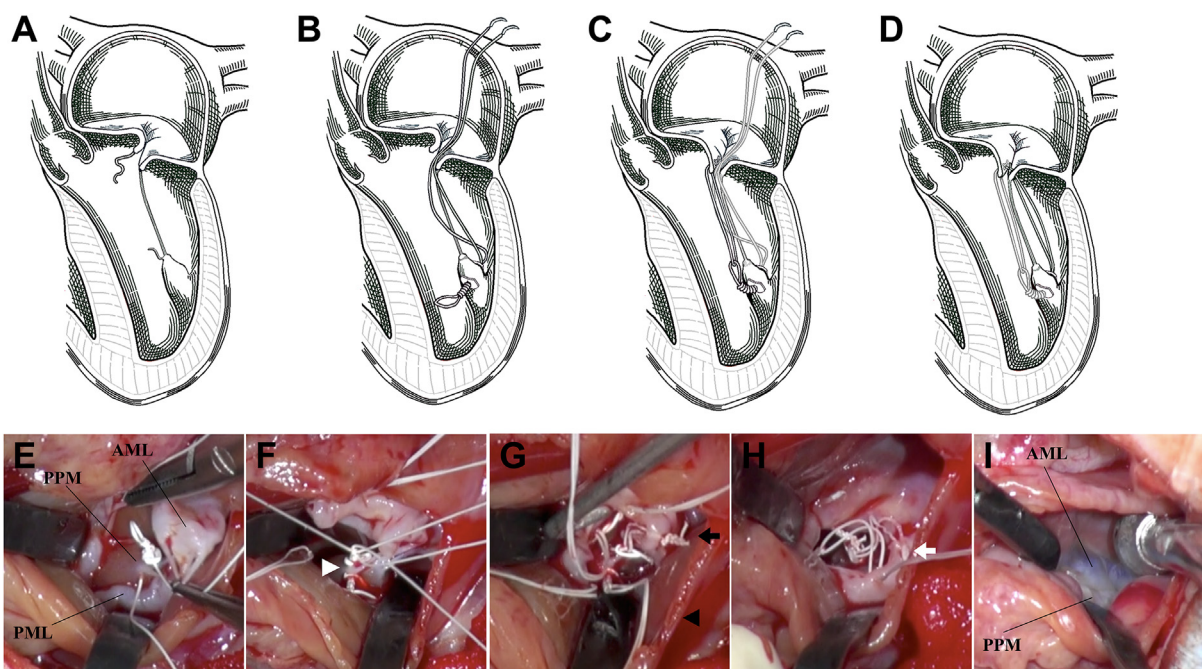
dimension (LA:Ao [reference,  $<1.6$ ]), left ventricular end-diastolic diameter [normalized for bodyweight] (LVIDDN [reference,  $<1.7$ ]), fractional shortening, diastolic transmitral flow velocity (E), and ratio of E to A (E:A) were measured as previously described [2–4]. The stage of MMVD was determined using the published criteria [1]. Patients require more than 8 mg/kg/day of furosemide or the equivalent dosage of other diuretics to control the clinical signs of heart failure was defined as Stage D. The severity of mitral regurgitation (MR) was categorized as 0 = none, 1 = trivial, 2 = mild, 3 = moderate, and 4 = severe, based on color flow Doppler echocardiography.

Surgery was performed under general anesthesia with the cardiopulmonary bypass undertaken as previously described [5]. Three incisions were made on the left side of the neck and chest and the right inner thigh. The carotid artery and jugular vein were bluntly dissected and cannulated to be connected to extracorporeal circulation. Invasive blood pressures were obtained from the femoral artery and vein. A fifth intercostal thoracotomy with pericardial tenting was performed to approach the heart. After surgery, the chest was closed, and the patient was gradually weaned from general anesthesia.

The loop-in-loop technique was used to adjust the height of each mitral leaflet [6]. The expanded polytetrafluoroethylene (ePTFE) loop anchor with a single small loop was made of a double-armed ePTFE suture<sup>a</sup> and a small ePTFE pledget<sup>b</sup>. Primary loop anchors two total were fixed on the anterior and posterior papillary muscles, respectively, with another ePTFE pledget. Next, a new CV-6 suture was passed through the primary loop sutured on the affected leaflet as a secondary loop, to adjust the length of the neochord (Fig. 1). The number of secondary loops depended on the status of the prolapsed area. In all cases, a modified DeVega semi-circular suture annuloplasty was subsequently performed using CV-6 or CV-5 sutures with small ePTFE pledgets [7]. Finally, a saline test

<sup>a</sup> CV-6; WL Gore & Associates Inc., Flagstaff, AZ, USA.

<sup>b</sup> Pledget E; Matsuda Ika-Kogyo, Tokyo, Japan.



**Figure 1** Illustration and intraoperative photograph of surgical technique. (A) The preoperative mitral apparatus showing the ruptured chordae tendineae between anterior mitral leaflet and papillary muscle. (B) After the resection of ruptured chordae, both arms of an anchor suture with a primary loop and pledget pass through the papillary muscle and are then tied over another pledget. (C) The secondary loop passes through the first loop and is then sutured on the affected anterior leaflet, adjusting the efficient length of the neochord. (D) Both arms of an anchor are used as the neochord of the posterior mitral leaflet. (E) An anchor suture with a small primary loop and a pledget is passed through the posterior papillary muscle. (F) The white arrowhead represents the anchor suture tied over another pledget. Note that two sutures have already been passed through the primary loop. (G) The black arrow shows a knot of the secondary loop on the rough zone of the anterior mitral leaflet. The black arrowhead points out the untied side of the anchor suture, which will be used as the neochord for the posterior mitral leaflet in the next step. (H) The white arrow indicates a knot tied to the posterior mitral leaflet. Note that another suture has been passed through the posterior mitral leaflet and has not yet been tied. (I) During the saline test, the pliability of the valve and residual leakage are assessed by saline injection into the left ventricle. The image shows appropriate coaptation of both the mitral leaflet and optimal alignment of the leaflet height without any backflow. AML: anterior mitral leaflet; PML: posterior mitral leaflet; PPM: posterior papillary muscle.

was conducted to confirm the quality of the valve function [8]. In cases where any inappropriate length of the neochord was recognized, the secondary loop was cut and/or added as appropriate. The recorded number of neochord on each papillary muscle was also reviewed.

### Statistical analysis

Statistical analyses were performed using R software version 4.0.2. The distribution of each variable was assessed using the Shapiro–Wilk normality test. Normally distributed data are shown as mean  $\pm$  standard deviations, while data not normally distributed are shown as medians and interquartile ranges. For comparison of variables at each time, the Tukey–Kramer test was used for normally distributed variables, while the Dunn test was used for variables that were determined to be

abnormally distributed. For survival analysis, Kaplan–Meier survival curves were used to assess the impact of the MMVD stage on cardiac death. Differences between groups were analyzed using the log-rank test, with the significance level set at  $P < 0.05$ .

### Results

Fifty-five cases were enrolled in this study. The loop-in-loop technique was used for all patients to reconstruct their mitral valve. The median body weight of the dogs was 4.0 kg (interquartile range 3.1–4.7 kg). In this study, 29 Chihuahuas, six mixed breed dogs, three Maltese, two Cavalier King Charles Spaniels, two Pomeranians, two Shiba Inu, two Shih Tzus, and one from each of the following breeds: American Cocker Spaniel, Beagle,

**Table 1** Preoperative and postoperative clinical variables for dogs undergoing surgical mitral valve repair with a loop-in-loop technique.

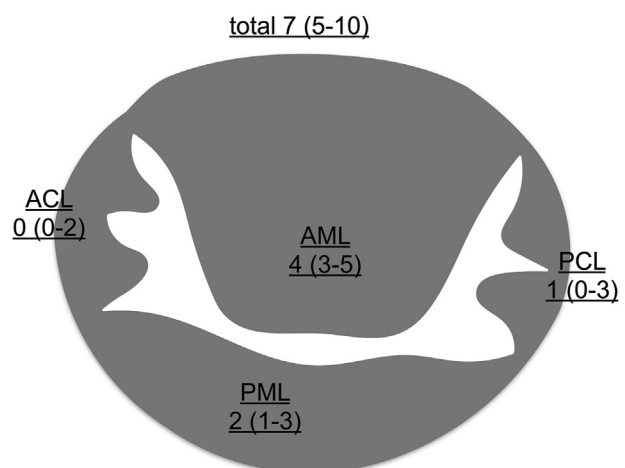
| Variables | Before surgery (n = 55) | 1 month (n = 50) | 3 months (n = 49) | 6 months (n = 44) | 12 months (n = 30) | 24 months (n = 12) |
|-----------|-------------------------|------------------|-------------------|-------------------|--------------------|--------------------|
| HR        | 156.8 (±28.8)           | 122.5 (±24.7)*   | 112.3 (±22.6)*    | 107.6 (±20.6)*    | 108.7 (±23.0)*     | 112.5 (±26.0)*     |
| VHS       | 11.4 (±1.0)             | 10.2 (±0.9)*     | 9.7 (±0.8)*       | 9.7 (±0.8)*       | 9.7 (±1.0)*        | 9.3 (±0.7)*        |
| LVDDN     | 2.2 (1.9–2.3)           | 1.5 (1.3–1.7)*   | 1.5 (1.3–1.6)*    | 1.5 (1.4–1.7)*    | 1.5 (1.4–1.6)*     | 1.3 (1.3–1.4)*     |
| LA:Ao     | 2.3 (±0.5)              | 1.5 (±0.3)*      | 1.4 (±0.2)*       | 1.4 (±0.2)*       | 1.4 (±0.1)*        | 1.3 (±0.1)*        |
| FS        | 51.1 (±8.8)             | 35.1 (±10.0)*    | 35.9 (±10.4)*     | 32.3 (±6.9)*      | 36.0 (±10.7)*      | 39.8 (±11.4)*      |
| E         | 1.3 (±0.3)              | 0.9 (±0.2)*      | 0.8 (±0.1)*       | 0.8 (±0.1)*       | 0.7 (±0.1)*        | 0.9 (±0.1)*        |
| E:A       | 1.8 (±0.8)              | 0.8 (±0.2)*      | 0.7 (±0.2)*       | 0.7 (±0.1)*       | 0.7 (±0.2)*        | 0.7 (±0.1)*        |

Mean ± standard deviation or median and interquartile range were shown. Tukey–Kramer test and Dunn test was used to compare variables at each timing depending on the normality of variables. P < 0.05 (\*) represent statistical significance compared with values before surgery. bpm: beats per minute; E: peak value of early diastolic transmitral flow velocity; E:A: ratio of E to A; FS: fractional shortening; HR: heart rate; LA:Ao: left atrium to aortic root ratio; LVDDN: left ventricular end-diastolic diameter [normalized for body weight]; VHS: vertebral heart score.

Chin, Miniature Dachshund, Miniature Schnauzer, Norfolk Terrier, Shetland Sheepdog, Toy Poodle, and Yorkshire terrier were included. The mean age was 10.3 (±2.3) years. Twenty-two were castrated male, 20 were intact male, nine were spayed female, and four were intact female. Clinical, radiographic, and echocardiographic variables are presented in Table 1. The pre-operative stage was Stage B2 in 14 cases, Stage C in 27 cases, and Stage D in 14 cases.

## Surgical outcome

Rupture of the chordae tendineae was documented in the majority of our population (44/55, 80.8%). The affected site was anterior in 26 cases (47.3%), posterior in five cases (9.1%), and both leaflets in 13 cases (23.6%). The number of implanted neochords totalled seven (five - 10), which were four (three - five) cords in the anterior, two (one - three) in the posterior, zero (zero - two) in the anterior commissure, one (zero - three) in the posterior commissure (Fig. 2). Total anesthesia time was 411 min, cardiopulmonary bypass time was 167 min, and the average aorta cross-clamping time was 109 min. There was no case of intraoperative death, though five cases died during hospitalization. Of these, one case was Stage C and the others were Stage D. The case with Stage C developed an interventricular septum hematoma (IVSH) immediately after the surgery, dying one day after the surgery due to heart failure. In this case alone, a necropsy was performed that confirmed the diagnosis of IVSH. One patient presented with sudden neurologic deficits



**Figure 2** A number of secondary loops are used for adjusting the height of each mitral leaflet. ACL: anterior commissural leaflet; AML: anterior mitral leaflet; PCL: posterior commissural leaflet; PML: posterior mitral leaflet. Numbers are shown as median (min–max).

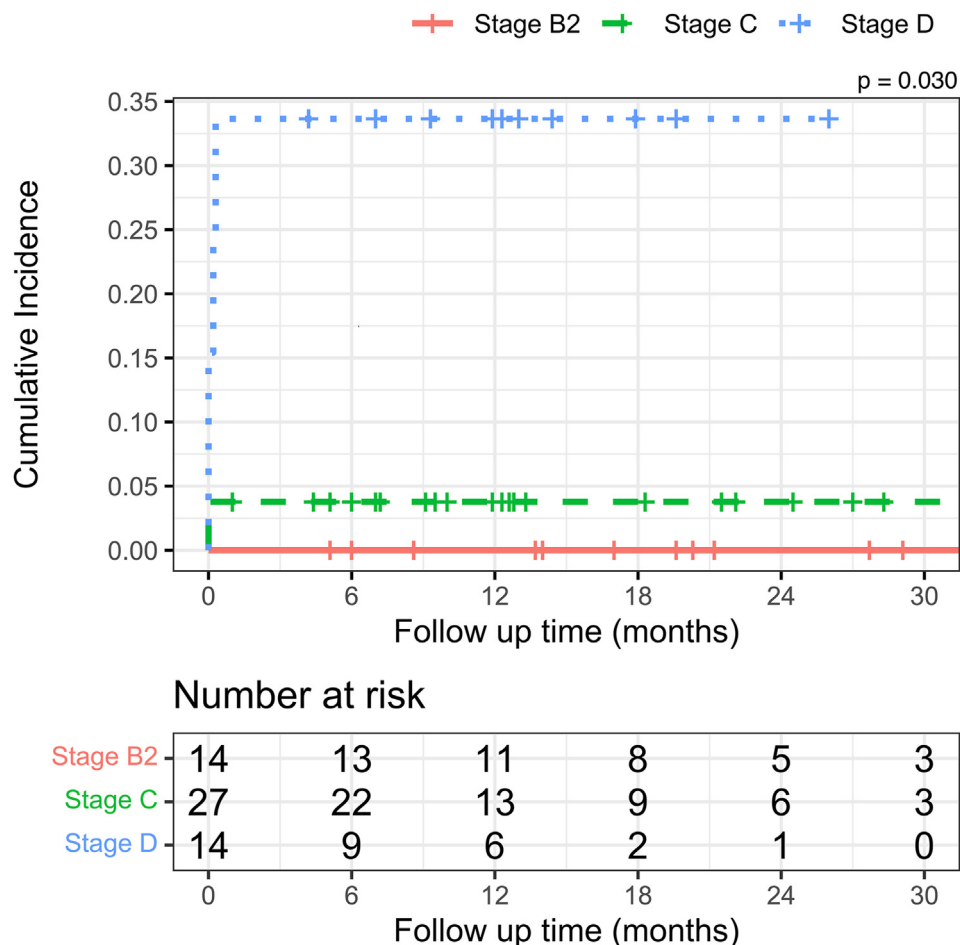


3 h after being weaned from general anesthesia and died the day after the surgery. Two patients developed atrial fibrillation (AF) at 8 and 10 h after surgery, respectively. Of these, one died of thrombosis one day after surgery, and the other died of hypotension due to heart failure nine days postoperatively. One patient that clinically deteriorated postoperatively died seven days after surgery from disseminated intravascular coagulation. These dogs died naturally and euthanasia was not performed in any cases. Another 50 cases survived to discharge. The total discharge rate was 90.9%, which was 100% in Stage B2, 96.2% in Stage C, and 71.4% in Stage D dogs. Complications that did not affect the prognosis included: acute renal failure (2), hemiplegia (1), seizure (1), pulmonary artery thrombus (1), left atrial thrombus (1), and necrosis of the digit (1).

Pimobendan 0.25–0.6 mg/kg per os (PO) twice daily (BID), rivaroxaban 0.5–1.6 mg/kg PO once daily (SID), amoxicillin clavulanate 20 mg/kg PO BID, and orbifloxacin 5 mg/kg PO SID for one week

were prescribed when dogs were discharged from the hospital. Angiotensin-converting enzyme inhibitors were discontinued immediately after surgery. Pimobendan was discontinued two weeks postoperatively in all dogs. Two patients determined to have interventricular septal flattening in end-systole before surgery continued to receive sildenafil 0.5 mg/kg PO BID. Excluding these two patients with pulmonary hypertension (PH), all other medications were discontinued except for rivaroxaban, which was administered for three months after surgery.

After surgery, MR was absent in 27 patients (49.1%), trivial in 24 patients (43.6%), and mild in four patients (7.2%). There were no reported cases of moderate or severe MR after surgery. Significant reductions of left atrium (LA/Ao: preoperative 2.3 vs. post one month 1.5,  $P < 0.001$ ) and left ventricle (LV/IDN: preoperative 2.2 vs. post one month 1.5,  $P < 0.001$ ) were documented one month after surgery, showing successful reduction of MR. Recurrent regurgitation, which leads to



**Figure 3** Kaplan–Meier curves illustrating cumulative incidence of cardiac-related death in dogs with MMVD Stage B2 ( $n = 14$ ), C ( $n = 27$ ), and D ( $n = 14$ ). The log-rank test revealed a significant difference in survival times between the groups ( $P = 0.030$ ).

cardiac remodeling or congestion, was not documented during the study period (Table 1). Preoperative E wave velocity was 1.3 m/s on average, which significantly decreased to 0.9 m/s postoperatively (Table 1).

Tricuspid regurgitation (TR) was observed in 37 cases, with a mean TR peak velocity of  $3.2 \pm 0.7$  m/s, which significantly decreased to  $2.9 \pm 0.5$  m/s postoperatively ( $P = 0.019$ ). Two patients with postoperative sildenafil therapy had higher peak TR velocities of 5.0 and 4.5 m/s preoperatively, decreasing to 3.1 and 3.3 m/s postoperatively. However, mild interventricular septal flattening in end-systole, right atrium enlargement, and notching of the Doppler right ventricular outflow profile were still evident after surgery.

During the hospitalization period, one dog with Stage C and four dogs with Stage D status died from postsurgical complications. During the follow-up period, three patients died of non-cardiac causes at times one, 20, and 24 months after surgery; two cases died from neoplasia and one from pancreatitis. The number of dogs that were alive (the denominator represents the total number of dogs reported based on when they were operated on relative to when data was analyzed) after surgery was 50/55 at one month, 49/49 at three months, 44/44 at six months, 30/30 at 12 months, and 12/12 at 24 months. Dogs with Stage D status had a decreased survival time compared to dogs with Stage B2 and C, according to survival analysis using Kaplan–Meier curves and the log-rank test ( $P = 0.030$ ) (Fig. 3).

## Discussion

Surgical mitral valve repair has shown a steady increase in success rates in the past two decades. Griffiths et al. reported that congestive heart failure resolved in nine of 18 dogs that underwent mitral valve repair in 2004 [9]. In a 2010 study, Kanemoto et al. [10] reported discharge after surgery in four of five miniature and toy breed dogs weighing less than 5.5 kg. Uechi et al. [11] reported that 45 of 48 small breed dogs weighing less than 5 kg were discharged after surgery, with 29 of them being free from medication in 2012. Advances in mitral valve repair made a great impact on MMVD treatment in small breed dogs. However, some clinical problems require addressing for improvement. For example, studies examining patient-specific surgical results such as the severity of MMVD and body weight are limited. Despite the wide range of severity of MMVD,

previous reports showed only total success rates [11]. Therefore, the success rate of surgery in relation to the severity of MMVD remains unclear. This information is necessary for veterinarians and owners to make clinical decisions on surgical indications. In addition, recent studies are limited to small breeds of dogs weighing less than 5 kg and, therefore, exclude breeds with a high incidence of MMVD, such as Cavalier King Charles Spaniels [10,11]. Furthermore, detailed descriptions of postoperative cardiac function are lacking in the current literature. Even in a report with a high surgical success rate, cardiac enlargement persists three months after surgery, with no further follow-up data [11]. Finally, cardiac medication was required in 36% of surviving cases, implying that some cases only achieved improved yet impaired cardiac function after surgery [11]. To address this lack of clinical knowledge on surgical mitral valve repair in dogs, this study includes all cases that underwent mitral valve repair, presenting postoperative echocardiographic variables for 24 months after surgery.

The present study described stage-specific success rates of mitral valve repair, which was 100% in Stage B2, 96.2% in Stage C, and 71.4% in Stage D MMVD dogs. Surgical mortality was observed in no dogs with Stage B2 and only one dog with Stage C. As also shown in the Kaplan–Meier curves, significantly higher perioperative mortality was observed in patients with Stage D MMVD. According to the disease stage-specific surgical results in this study, surgical mitral valve repair is a good treatment of choice for dogs with Stage B2 and C MMVD. Although dogs with Stage D demonstrated a relatively high mortality rate during the perioperative period, no cardiac death was observed more than 2 weeks after surgery, as shown in the Kaplan–Meier curves. Within the observation period in this study, cases that survived surgery had a good prognosis regardless of preoperative MMVD severity. Thus, considering the estimated short survival time in advanced-stage MMVD cases, surgical treatment can be indicated for Stage D dogs, after carefully informing the owners of the risks involved.

About 1/4 of the cases include medium-sized dogs weighing 5–12 kg, which have previously not been reported on to date. Our data showed that the inclusion of these medium-sized dogs did not significantly affect the success rate of this surgery compared to the previous report [11].

Serious complications that resulted in poor outcomes were peculiar to open-heart surgery such as AF, thrombosis, neurological disturbance, and IVSH. Two patients with MMVD Stage D developed AF after surgery, one died of associated

thrombosis, and the other due to heart failure. Atrial fibrillation is triggered by excessive extension of the LA and a thinned LA wall can be associated with decreased LA function, resulting in thrombus formation in the LA [12]. Thus, one of the reasons for the relatively low survival rates of dogs with Stage D MMVD may be related to preoperative excessive congestion, which induces hyperextension of the left atrium. These high LA pressure should be mitigated preoperatively to improve surgery results. Atrial septum puncture was presented as a left atrial decompression method [13]. By reducing left atrial pressure in advance of open-heart surgery, critically ill patients could temporarily escape the highest risk period. Surgery during a stable period may lead to improved surgical outcomes. In other words, atrial septum puncture may be a good bridge to valve repair surgery for advanced-stage patients who cannot undergo immediate surgical intervention. In both dogs and humans, patients with preoperative AF and an enlarged LA are at risk for postoperative AF [14]. Left atrial appendage occlusion is commonly performed during cardiac surgery to reduce the risk of thromboembolic events in humans with an enlarged LA. This procedure can also be considered for dogs with an enlarged LA [15].

Another serious complication was thrombosis. Possible factors of thrombosis during the early stages of postoperative recovery include (1) thrombosis, associated with the use of cardiopulmonary bypass, (2) endocardial injury, and (3) intracardiac stagnation of blood flow due to decreased cardiac function [16]. Two cases in this study died from suspected thrombosis in the early postoperative period. These patients were not diagnosed with prothrombotic diseases, i.e. hyperadrenocorticism vs. protein losing enteropathy vs. others, and the cause of life-threatening postoperative thrombotic events remains unknown. To predict the risk of thrombosis in patients undergoing mitral valve repair, further large-scale studies should be conducted. In the later postoperative period, sutures and pledgets can act as foreign bodies that may result in valvular thrombosis. Antithrombotic treatment is necessary for three months to prevent thrombosis after valvular surgery in humans and dogs [17,18]. In our cases, no cases of thrombosis occurred more than three months after the surgery, supporting the previous study's findings.

The optimal antithrombotic treatment protocol after mitral valve repair in dogs is unknown. Rivaroxaban has recently been shown to be safe and effective as an antithrombotic treatment after

MR surgery in humans [19]. Rivaroxaban is also used in dogs to prevent thrombosis, but the effective antithrombotic dose and protocol vary depending on the age and medical condition of the patient [20]. At large, we prevented postoperative complications associated with thrombosis, despite our need for an abundance of sutures during surgery. However, one case with asymptomatic intraatrial thrombus and the other case with necrosis of the digit were observed, suspected to be the result of peripheral thromboembolism. Further research is needed to determine the optimal dosage of rivaroxaban after canine mitral valve surgery.

A patient with neurological dysfunction died one week after surgery. Neurological abnormalities are also documented in the report by Kanemoto et al. [10]. A complication was documented in one patient with a history of hydrocephalus. Postoperative computed tomography was not performed; therefore, the exact cause of the patient's complication was not identified. It is unclear whether asymptomatic hydrocephalus is a risk factor for neurological disturbance associated with mitral surgery.

One patient with Stage C MMVD developed IVSH and died the day after surgery due to heart failure. Dogs with IVSH have been reported here and in a previous study [21]. The cause of IVSH is still unclear in dogs and humans [21,22]. The incidence was not higher than previously reported and IVSH occurs in humans with various conditions such as chest trauma, myocardial infarction, and various cardiac surgeries. Thus, IVSH was not considered to be specific to the procedure used in this study.

The velocity of TR was decreased after the surgery. This shows that pulmonary venous hypertension was the major cause of preoperative PH. However, in very few cases, the normalization of pulmonary vein pressure did not cure PH. In these cases, irreversible vascular remodeling may have occurred in the pulmonary arteries. If preoperative pulmonary vascular characteristics can be accurately identified before surgery, it may help predict residual PH after surgery. A new non-invasive method for the classification of PH has been reported; further study verifying its utility as a method for predicting postoperative residual PH is warranted [23,24]. In addition, it is imperative to inform owners that medication may be required after surgery for patients with preoperative PH. Further research is needed to optimize the duration and dose of the drugs against postoperative PH.

Postoperative X-ray and echo imaging is important for understanding the condition of the heart.

A large heart early after surgery represents residual regurgitation or decreased cardiac function. In addition, the progress of cardiac enlargement in the remote period after surgery indicates that the durability of surgery is low. Previous studies on this surgery have not shown imaging data or only closed echo data for up to three months and have inadequately described the postoperative cardiac conditions [10,11]. In this study, we described postoperative VHS and echocardiographic variables such as LA/Ao and LVDDN for 24 months after surgery. One month was enough for the heart to reduce its size within the reference range, such as LA/Ao < 1.6, LVDDN < 1.7, and VHS < 10.6, reflecting the feasibility of the loop-in-loop technique. This is clearly different from a previous report showing a higher LA/Ao of 1.8 and VHS of 11, one month after surgery [11]. The high drug-free rate (96%) in this study also showed significant improvement in postoperative cardiac function compared to previous reports [11]. The difference in surgical technique may be one of the important factors affecting this discrepancy. The loop-in-loop technique is characterized by creating a number of neochord by passing an additional thread through the primary loop on the anchor. It facilitates the application of many reconstructed threads, as the additional reconstruction does not further damage the papillary muscles. This technique was suitable to mitigate volume loading and pathological cardiac enlargement during the early stages after surgery.

In addition to mitral cord implantation, suture annuloplasty was applied to our cases. As shown in a previous study with an average follow-up period of 32.8 months, the durability of the suture annuloplasty was confirmed by our data, in which no case had recurrent cardiac enlargement after surgery [10]. Low postoperative transmitral gradients indicated that there were no cases of severe congestion or stenosis. As a result, no patients required cardiac medications due to left-sided heart disease. Thus, our data showed that recurrence and failure in repair were not major concerns of our technique. Pimobendan and angiotensin-converting enzyme inhibitors were discontinued after surgery. Even in cases where the follow-up period has passed by years, the technique did not lead to recurrent cardiac enlargement. Such findings are consistent with a previous report, showing a marked postoperative decrease in neurohormonal activation and good reverse remodeling without renin-angiotensin-aldosterone blockade medication, three months after canine mitral valve repair [25]. The main

concern of the loop-in-loop technique is the prolonged time of the intracardiac procedure. It leads to a longer duration of cardiac arrest compared to other techniques [10]. Longer arrest time may potentiate postoperative cardiac dysfunction. However, our results showed no cases of low output syndrome or clinically relevant myocardial ischemia due to the longer arrest time. Mihara et al. [26] report long aortic clamping times to repair extensive valve lesions. As is also mentioned in the other review article, we need to study advanced cardioplegic procedures that allow us to repair complicated multiple valve lesions in canine MMVD [8].

The study showed the results of the loop-in-loop technique. However, since this technique has not been compared with other methods, it is unclear to what extent this performance will vary depending on the procedure. The position of the anchor, the number of artificial chordae tendineae, the length of the neochord, and the diameter of the annuloplasty are all factors that dictate the surgical experience. The major limitation of this method is the uncertainty in this important regard. Overcoming these uncertainties requires a system that can be broadly adapted to the variability of the individual heart anatomy, which is also an ongoing issue in human medicine.

In this study, the assessment of MR severity was based solely on color flow Doppler which can be subject to technical issues and bias. Quantitative analysis should be conducted in a future study to verify the severity of residual MR in detail.

In terms of the durability of the loop-in-loop technique, the longest echocardiographic follow-up was taken at 1,000 days, and close follow-up at more distant postoperative times is warranted. Although the two-year outcome of the loop-in-loop technique has been promising, it is necessary to re-evaluate the durability in future follow-ups.

## Conclusions

This study showed that the surgical results of mitral valve repair are significantly reduced in dogs with MMVD Stage D. In other words, a successful result can be achieved in dogs with earlier stages of MMVD. These results provide critical insight into clinical decision-making. In addition, preoperative and postoperative radiographic and echocardiographic changes revealed that our technique was feasible to normalize the size of the heart, even one month after surgery. Normalized heart size was found to be maintained yearly, suggesting the durability of the repaired mitral valve.



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